Videodensitometric analysis of human coronary stenoses: validation in vivo by intraoperative high-frequency epicardial echocardiography

MARYL R. JOHNSON, M.D., DAVID D. MCPHERSON, M.D., STEVEN R. FLEAGLE, B.S.E.E., MICHELLE M. HUNT, B.S., LOREN F. HIRATZKA, M.D., RICHARD E. KERBER, M.D., MELVIN L. MARCUS, M.D., STEVE M. COLLINS, PH.D., AND DAVID J. SKORTON, M.D.

ABSTRACT Videodensitometry is a nongeometric method of coronary angiographic analysis that can be used to provide an index of coronary luminal area. However, there are few direct studies in vivo of the relationship of videodensitometric data to independent measures of luminal area in humans. Although videodensitometry is theoretically independent of angiographic projection and luminal shape, validation of these assumptions in vivo is also limited. We therefore used intraoperative high-frequency epicardial echocardiography, a technique that can directly determine human coronary luminal area and shape in vivo, to further validate videodensitometry. A total of 36 arterial segments in the left anterior descending and right coronary arteries were studied by videodensitometry and high-frequency echocardiography. Videodensitometry was performed on angiograms in which the arterial segment of interest was not markedly foreshortened and was uniformly filled with contrast. In 22 discrete lesions (13 with circular lumens and nine with oval or complex lumens), videodensitometric and echocardiographic measures of luminal area correlated well (r = .86). In 33 coronary arterial segments, the effect of angiographic projection on videodensitometry was determined by comparison of the results of videodensitometry performed on left anterior oblique vs right anterior oblique angiograms of the segments. Here too, the correlation was good (r = .94, y = 1.04x + 0.002). The good correlation of left anterior oblique with right anterior oblique videodensitometric results held true for lesions with circular and oval or complex lumens. This study further validates the ability of videodensitometry to provide an index of coronary luminal area and confirms in vivo previous assumptions that the results of videodensitometric analysis are independent of angiographic projection and luminal shape.


RECENTLY, substantial investigative effort has been directed toward developing approaches to better assess the anatomic and physiologic significance of coronary lesions based on their angiographic appearance. This effort has stemmed from increasing recognition of problems associated with the standard method of angiographic analysis, that of visually estimating percent diameter stenosis. Measurements of percent stenosis may be associated with substantial intraobserver and interobserver variability.1–3 In addition, measurements of percent stenosis in patients with multivessel coronary artery disease may not correlate with coronary lesion geometry, as defined by the method of quantitative coronary arteriography described by Brown et al.,4 or lesion physiologic significance, as defined by intraoperative Doppler reactive hyperemia studies.6,7

Percent stenosis may not accurately reflect lesion physiologic significance because the angiographically “normal” segment of the coronary artery may not be free of atherosclerotic disease. This has been shown in pathologic studies,8,9 and we have recently confirmed that diffuse coronary disease is present in some human coronary arterial segments that appear normal or nearly normal on coronary angiograms.10 Thus, an absolute rather than relative measure of luminal area may be a better predictor of coronary lesion physiologic significance. Indeed, previous studies have shown that the
minimal luminal cross-sectional area is one of the most important determinants of lesion physiologic significance.\textsuperscript{11}

Geometric methods can define absolute size of the coronary lumen. We have shown that absolute luminal sizes determined with geometric methods (such as quantitative coronary arteriography or computer-based edge definition followed by determination of arterial minimal diameter) correlate much better with coronary lesion physiologic significance than do measures of percent stenosis.\textsuperscript{7, 12, 13} However, geometric methods depend on exact definition of vessel edges and require assumptions as to luminal shape. Therefore, inaccuracies might occur in the evaluation of lesions with indistinct vessel edges or irregular luminal shapes. Although investigators have been working to make geometric methods of angiographic analysis easier and faster,\textsuperscript{14} many geometric methods remain time consuming and difficult, and cannot be readily applied at the time of cardiac catheterization.

Videodensitometry is a nongeometric approach to the analysis of coronary cineangiograms. Videodensitometry consists of measurement of the x-ray attenuation through a contrast-filled coronary artery and from this information estimating the amount of contrast in the vessel, which is an index of luminal size.\textsuperscript{15} Videodensitometry is potentially advantageous for the evaluation of human coronary cineangiograms for several reasons. First, it can be used to estimate an absolute as well as relative (i.e., percent stenosis) index of coronary luminal size.\textsuperscript{16–19} In addition, videodensitometry is not dependent on exact definition of vessel edges and is theoretically free of assumptions as to shape of the lumen. Such characteristics may be important in analyzing lesions immediately after thrombolysis or angioplasty, when vessel borders are indistinct and the luminal shape is irregular.\textsuperscript{20} Finally, videodensitometric analysis is simple and can be rapidly applied, particularly to digital coronary angiographic information, which is becoming more widely available.

We have reported that the results of videodensitometric analysis of lesions in all three coronary arteries correlate well with coronary luminal area, as defined by quantitative coronary arteriography by the method of Brown et al.,\textsuperscript{5} and with lesion physiologic significance, as defined by Doppler studies of vasodilator reserve.\textsuperscript{16–19} However, before videodensitometry can be recommended for widespread clinical application, more specific, assumption-free validation in humans in vivo is necessary.

High-frequency epicardial echocardiography is an intraoperative, ultrasonic technique that provides tomographic images of the coronary arteries. These tomographic images allow direct visualization of coronary arterial lumens and walls, and from the images accurate and reproducible measurements of coronary lesion luminal areas, diameters, wall thicknesses, and shapes can be made.\textsuperscript{21} Luminal areas defined by high-frequency echocardiography are not dependent on assumptions of a particular luminal shape as are many of the geometric methods of angiographic analysis.\textsuperscript{5} For this reason, we chose high-frequency epicardial echocardiography as a nonangiographic method of further validating in vivo the ability of videodensitometry to provide an index of coronary luminal area. In addition, although videodensitometry is theoretically independent of angiographic projection and luminal shape, proof of this assumption in vivo is limited. High-frequency echocardiography allows analysis of coronary luminal shape. Therefore, we also used this technique to evaluate the effect of angiographic projection and luminal shape on the results of videodensitometric analysis.

**Methods**

**Patient population.** One-hundred eight coronary arterial segments in 47 patients had been evaluated by use of high-frequency echocardiography and were available for consideration for inclusion in this study. Fifty-five segments were excluded because no discrete lesion was seen on the corresponding coronary angiogram. In eight cases, the segment studied with high-frequency echocardiography was distal to an angiographic total occlusion. In one case, the segment studied with echocardiography was distal to a subtotal occlusion and showed competitive flow (antegrade and collateral) on the angiogram. One segment was excluded due to the presence of calcium in the lesion, four due to incomplete opacification on the angiogram, and three due to vessel overlap on the angiogram. The remaining 36 coronary arterial segments in 23 patients were included in the study.

Of the 23 patients in the study, all but two had multivessel coronary artery disease. (Considering lesions greater than 50% diameter stenosis as significant, 16 patients had three-vessel disease, five patients had two-vessel disease, one had one-vessel disease, and one had no lesions greater than 50%.) To be included in the study, patients had to have angiographically defined disease in the left anterior descending or right coronary artery. Although many of the patients had significant lesions in the circumflex coronary artery as well, these could not be studied by ultrasound due to the posterior location of the artery and the size of the high-frequency echocardiographic probe currently used (20 cm long, 2 cm wide). Coronary angiograms of the arterial region of interest had to be adequate for evaluation by computerized videodensitometry (that is, angiograms had to show the arterial segment with the plane of the vessel as parallel to the image intensifier as possible and the artery uniformly filled with contrast). The patients also had to have good quality, high-frequency epicardial echocardiographic images of the arterial segment of interest. For the portion of the study in which the effect of angiographic projection on videodensitometric data was evaluated, there also had to be adequate angiographic studies of the arterial region of interest in nearly orthogonal (left
anterior oblique and right anterior oblique) views. That is, left anterior oblique and right anterior oblique angiograms showing the arterial segment of interest nearly parallel to the image intensifier and uniformly filled with contrast had to be available. (Cranial or caudal angulated views were necessary to meet these criteria in 13 of the vascular segments included in the study.) All patients gave informed consent before the high-frequency epicardial echocardiographic studies. The protocol for intraoperative echocardiographic study of human coronary arteries was approved by the Human Subjects Review Committee of the University of Iowa.

**Videodensitometric analysis**

**Coronary angiography.** Premedications in the 23 patients included 0.6 mg sc atropine (in 19 patients), a mild sedative (diazepam in 20 patients, secobarbital in one patient), and an antihistamine (promethazine in 15 patients, diphenhydramine in six patients). Nitroglycerin (0.4 mg sublingual) was given to 16 of the patients immediately before coronary angiography. Four of the patients received sublingual nifedipine in the catheterization laboratory. Coronary angiography was performed by the percutaneous femoral technique described by Judkins. 22 The electrocardiogram and central aortic pressure (measured through a contrast-filled coronary catheter) were recorded just before and after each coronary cineangiogram. Angiograms were obtained in multiple, single-plane projections with use of a Siemens x-ray system with a 7 inch image intensifier (20 patients) or a Philips system with a 6 inch image intensifier (three patients). Angiograms were recorded on 35 mm cine film at 60 frames/sec. Film processing was carefully controlled. End-diastolic angiographic frames showing the arterial region of interest well opacified with contrast and as nearly parallel to the image intensifier as possible were selected for videodensitometric analysis.

**Computerized coronary videodensitometry.** Videodensitometric analysis was performed as previously described by our group. 16 Cine frames were digitized by use of a modified Vanguard cine film transport. The projected angiographic image was coupled through selected optical lenses to a high-quality vidicon camera (Cohu Model 8000). Cine frames were digitized by a DeAnza 8500 image-array processor interfaced with a PDP 11/44 computer.

Before digitization of individual cine frames, the sensitivity of the vidicon camera (target control) was adjusted to prevent saturation in the brighter portions of a typical image and to ensure a wide dynamic range in the digitized image. At this camera setting, calibration data relating mean gray level (digitized value) and optical density of the film were measured with a Kodak gray level step wedge with 21 optical density levels distributed uniformly between 0.05 and 3.10. This range encompassed the film densities we observed. These data were entered into the computer, and a continuous calibration curve was calculated by linear interpolation. Individual cineangiographic frames were then digitized at a magnification of 3.7 times 512 times 512 pixel matrix with 8-bit (256 levels) gray level resolution. (This represents a digitization resolution of about 0.06 mm/pixel, depending on the geometric magnification at which the angiogram was obtained.) The digitized images were subsequently displayed on a video monitor for videodensitometric analysis with use of an operator-interactive program. The images were analyzed by an observer who was unaware of the results of the high-frequency echocardiographic analysis.

The operator identified the approximate centerline of the arterial segment of interest and the length of the segment to be analyzed. The computer then calculated and displayed an average gray level profile from left to right across the artery perpendicular to the centerline. Using this profile as an aid, the operator identified the arterial borders as well as background regions on both sides of the artery. The gray level profile for each lesion was converted to an optical density profile with the use of the previously determined calibration curve. The optical density for each point on the profile within the artery was corrected for the optical density of the corresponding background point defined by linearly interpolating between the average optical density values for the background regions on both sides of the artery. An integrated optical density value for the arterial segment of interest was obtained by summing the resultant background-corrected optical densities over all points within the artery. This value was reported in optical density units. Ignoring the effects of x-ray scatter and assuming that the image intensifier operates linearly, that image data are recorded in the linear portion of the film characteristic curve, and that there is uniform mixing of contrast media and blood in the arterial lumen, this measure of integrated optical density is proportional to luminal cross-sectional area. We have previously found that values of integrated optical density determined in this way have good intraobserver (r = 0.98) and interobserver (r = 0.87) reproducibility. 17

For vessels included in the portion of the study assessing the effects of angiographic projection on videodensitometric results, the above analysis was performed by the same observer on orthogonal angiographic projections of the coronary arterial segment of interest.

**High-frequency epicardial echocardiography**

**Intraoperative protocol.** Patients taken to the operating room for elective open heart surgery were managed according to standard operative procedures. They were anesthetized, intubated, and ventilated with a mechanical respirator. A variety of anesthetic agents was used, including nitrous oxide, halothane, morphine, and fentanyl. Radial artery pressure and the electrocardiogram were recorded and left atrial pressure was continuously monitored. All operations were performed through a midline sternotomy. Just before the echocardiographic studies, intravenous heparin was administered to raise the activated clotting time to 480 sec or more. Preparations were made to institute cardiopulmonary bypass should hemodynamic instability occur; however, all patients remained hemodynamically stable during the echocardiographic studies.

A Biosound Surgiscan unit (Biosound Inc., Indianapolis) with a 12 MHz probe was used to obtain the coronary arterial images. The ultrasonic probe was sterilized with a standard 130°C ethylene oxide sterilizing procedure for an 18 hr cycle before intraoperative use.

The surgeon scanned the diseased segments of the left anterior descending and right coronary arteries in cross and longitudinal section with the hand-held, high-frequency echocardiographic probe. Probe location was referenced to external landmarks, primarily vessel branch points, and imaging of diseased arterial segments in cross section was emphasized. (As noted previously, the circumflex coronary artery could not be scanned due to the size of the echocardiographic probe.) Ultrasound system gains were adjusted to make the interface between the arterial lumen and the intima as sharp as possible without blooming of the intima into the lumen. As the ultrasonic probe was moved along the diseased coronary segment, echocardiographic images (including a 3 mm calibration bar) were recorded on videotape for subsequent playback and analysis. Probe location was also described and recorded.

**Image analysis.** Analysis was limited to high-quality, cross-sectional arterial images. Freeze-frame arterial images were analyzed with an IREX (IREX Med. Systems, Ramsey, NJ) digitizing system. The echocardiographic image was displayed in cross section at the point in the cardiac cycle when the arterial diameter appeared largest.

For measurement purposes, the inner edge of the bright interface between the coronary lumen and the intima was identified
and the lumen was outlined on the luminal side of this interface. From this outline, luminal area was directly calculated. Four luminal diameters at equiangular intervals (i.e., every 45 degrees) around the circumference of the lumen were measured. With these diameter measurements, luminal shape was classified by calculating the maximum to minimum luminal diameter ratio. Lumens having a maximum to minimum diameter ratio of less than 1.5:1 were considered by convention to be circular, those with a ratio of greater than 1.5:1 were considered oval, and markedly irregular lumens were classified as complex. Examples of echocardiographic images of lesions with circular, oval, and complex lumens are shown in figure 1. Although multiple freeze-frame images along the diseased coronary segment were analyzed, only those frames showing the lumen with the smallest cross-sectional area were used for the comparisons made in this study.

**Study protocol and data analysis**

**Videodensitometry vs echocardiographic luminal area.** The integrated optical densities of arterial segments with single, discrete lesions on the angiogram were compared with measurements of minimal coronary luminal area defined by high-frequency echocardiography of the same arterial segments. Only arterial segments with single, discrete lesions were included in this portion of the study so that the segment of the artery analyzed by videodensitometry and high-frequency echocardiography could be matched as precisely as possible. Analyses were performed for the entire group of lesions studied, including lesions with luminal shapes defined as both circular and oval/complex. The comparison of integrated optical density vs echocardiographic luminal area was performed by linear regression analysis.

**Effects of angiographic projection and luminal shape.** In arterial segments for which left anterior oblique and right anterior oblique orthogonal angiographic projections of the arterial segment of interest suitable for videodensitometry analysis were available, the results of videodensitometry performed on the left vs the right anterior oblique projection were compared. This analysis was performed to determine if the specific angiographic projection, i.e., left anterior oblique versus right anterior oblique, affected the results of videodensitometric analysis. In addition, to determine whether the effect of projection on videodensitometric data was affected by luminal shape, similar analyses were performed in the subgroups of arterial segments defined as having circular and oval/complex lumens on the high-frequency echocardiogram. All analyses were performed with linear regression techniques. The slopes and intercepts of the regression lines calculated for the comparison of videodensitometric results in different projections were compared with one and zero, respectively, by use of t statistics.

**Results**

**Patient characteristics.** A total of 36 arterial segments (12 in the left anterior descending coronary artery and 24 in the right coronary artery) in 23 patients were evaluated. The study population included 15 men and eight women with ages ranging from 35 to 76 years and a mean age of 58 years. The interval between cardiac catheterization and surgery varied from 2 days to 16 months, with a mean interval of 36 ± 9 (mean ± SD) days. In all but three patients the interval between catheterization and surgery was less than 1 month, and in all but one patient the interval was less than 3 months. At the time of coronary angiography, mean systemic blood pressure was 77 ± 2 mm Hg (mean ± SEM) and mean heart rate was 75 ± 2 beats/min. At the time the high-frequency echocardiographic studies were performed in the operating room, mean blood pressure was 76 ± 2 mm Hg and mean heart rate was 71 ± 2 beats/min. The hemodynamic values during angiography were not significantly different from those recorded intraoperatively (p = NS, paired t test). Seventeen patients were taking β-blockers, 14 patients calcium-channel blockers, and 14 patients nitrate preparations at the time of cardiac catheterization. Just before surgery, 20 patients were on β-blockers, 18 patients were on calcium-channel blockers, and 16 patients were using nitrate preparations. Twenty-two discrete lesions in 18 patients were evaluated in the portion of the study evaluating the ability of videodensitometry to define an index of luminal area. Echocardiographic minimum luminal area varied from 0.2 to 6.1 mm² in these lesions of which 13 were classified as circular, eight as oval, and one as complex. Thirty-three arterial segments in 21 patients were studied to evaluate the effect of angiographic projection on videodensitometry. Of these 33 arterial segments, 19 were classified as having circular lumens, 11 were classified

**FIGURE 1.** Examples of echocardiographic images of lesions with circular (left), oval (center), and complex (right) lumens. Ath = atheroma; L = lumen.
as having oval lumens, and three were classified as having complex lumens. (Nineteen arterial segments in 16 patients were included in both portions of the study.)

**Videodensitometry vs echocardiographic luminal area.**

The relationship between videodensitometric and echocardiographic measurements of coronary lumen area is shown in figure 2. For all 22 lesions, a correlation coefficient of $r = .86$ was noted for the relationship between integrated optical density defined by videodensitometry and luminal area defined by high-frequency echocardiography. The correlation coefficients for the relationship between integrated optical density and echocardiographic luminal area in the subgroups of the 13 circular lesions (circles) and the nine oval or complex lesions (triangles) were $r = .81$ and $r = .93$, respectively.

**Effects of angiographic projection and luminal shape.**

The correlation noted between integrated optical density values defined in the left anterior oblique and right anterior oblique angiographic projections is shown in figure 3. In the 33 arterial segments, the correlation coefficient for this relationship was .94, with a regression line of $y = 1.04x + 0.002$. This slope and intercept did not significantly differ from one and zero, respectively. Thus, regardless of whether the angiograms analyzed were taken in a left anterior oblique or right anterior oblique projection, the results obtained for videodensitometric analysis of the lesions were similar.

Figure 3 also shows that the good correlation between integrated optical densities defined by videodensitometric analysis in two orthogonal angiographic projections holds true for both circular lesions (circles) and oval/complex lesions (triangles). For the 19 circular lesions, the correlation coefficient was .95, with a regression line of $y = 0.98x + 0.080$. Similarly, for the 14 oval/complex lesions, the correlation coefficient was .94, with a regression line of $y = 1.09x - 0.022$. The slopes and intercepts of these relationships were not significantly different from one and zero, respectively. Thus, even in lesions with oval or complex shapes, for which geometric measurements of luminal size in different projections might be variable, videodensitometry gives the same results in orthogonal angiographic projections and therefore is independent of luminal shape.

**Discussion**

The major findings of the present study are that: (1) videodensitometric analysis provides a reasonable index of coronary lesion luminal area as defined with a nonangiographic, in vivo measurement technique (high-frequency epicardial echocardiography), and (2) the results of videodensitometric analysis are independent of angiographic projection, as long as the vascular segment of interest is nearly parallel to the image intensifier, and independent of luminal shape as defined by high-frequency epicardial echocardiography.

**Prior videodensitometric studies.** Other investigators have reported on the feasibility and accuracy of the use of videodensitometry to estimate coronary luminal size. Krugert23 has reported that direct density measures can be used to accurately define absolute and relative
vessel diameters in Plexiglas and aluminum vessel phantoms. Similar data have been obtained by Nichols et al. for relative densities (i.e., percent stenosis) of the stenotic and “normal” arterial segments in phantoms and postmortem human hearts. Wiesel et al. have used a videodensity method to define absolute luminal areas in cylindrical phantoms and in Delrin cylinders placed in dog coronary arteries. Tobis et al. have reported the use of videodensitometry to define absolute luminal diameters in lucite phantoms filled with contrast. Mancini et al. have correlated densitometric determinations of luminal area in a dog preparation of coronary stenosis with independent measures of coronary flow reserve. Our previous work has shown that the results of videodensitometric analysis of human coronary stenoses correlate well with coronary luminal area, as defined by quantitative coronary arteriography (method of Brown et al.), and lesion physiologic significance, as defined by Doppler studies of vasodilator reserve. However, the present study provides the most direct validation of the videodensitometric technique in humans in vivo that is currently available.

Theoretically, videodensitometry should be independent of angiographic projection and luminal shape. Nichols et al. and Tobis et al. have reported that determinations of percent stenosis derived from densitometric data are similar whether defined on the left anterior oblique or right anterior oblique angiogram. (In the Tobis study, the right anterior oblique/left anterior oblique correlation for videodensitometric percent stenosis was similar to that for geometric percent stenosis.) However, study of the effects of angiographic projection on the derivation of indexes of absolute luminal area by videodensitometry has been limited. Likewise, determination of the effects of luminal shape on videodensitometric results in vivo has not previously been reported.

**Potential limitations of this study**

*Limits of videodensitometry.* Videodensitometric analysis is based on the Lambert-Beer law, which assumes that there is a direct relationship between the mass of radioopaque material in a certain portion of the vascular system and fractional x-ray transmission. Unfortunately, the Lambert-Beer law is an idealized model of the interaction between the x-ray beam and the contrast-filled vessel and does not take into account the effect of certain technical factors on videodensitometric analysis. These factors include beam hardening and x-ray scatter (which result directly from the process of x-ray generation and x-ray interaction with the subject) as well as “veiling glare” (which results from light scatter and multiple reflections within the image intensifier and the optics of the imaging system). Variation in focal spot size may also modify the observed videodensitometric profile. Other investigators have attempted to develop correction factors for some of these variables, and phantom studies suggest that the degree of inaccuracy resulting from these factors is small. However, little is known about the effect of these factors on the evaluation of human coronary stenoses, where the effect of such technical variables may be greater, and these factors may have accounted for some of the variability in our results.

Another potential problem with videodensitometry is that variable contrast concentrations may occur within the vessel lumen, resulting from variability in injection techniques or in the rate of coronary blood flow. Since videodensitometry assumes a direct relationship between the mass of radioopaque material within the vascular lumen and fractional x-ray transmission, the concentration of contrast medium will affect videodensitometric results. Phantom studies have shown a linear relationship between the concentration of contrast medium and density measurements. In our clinical studies, we have simply analyzed arteries that appear to be uniformly well opacified with contrast and we have obtained good correlations between the results of videodensitometry and quantitative coronary arteriography, Doppler studies of vasodilator reserve, and high-frequency echocardiography. However, our correlations may have been better, and the scatter in our data less, had we been able to control the uniformity of contrast in the arterial lumen.

Another concern is that angulation of the vessel relative to the image intensifier may significantly affect videodensitometric results. Clearly, analysis of a vessel “end-on” would not result in an accurate determination of lumen area because the x-ray attenuation would be produced by contrast present in a “length” rather than a “cross section” of the vessel. Thus, in our studies we have chosen angiographic projections in which the arterial segment of interest appears parallel to the image intensifier. However, the degree of angulation of the vessel relative to the image intensifier that results in significant inaccuracies has not been defined. In a preliminary study we found that the results of videodensitometric analysis of proximal left anterior descending lesions in the right anterior oblique projection correlated quite well with lesion geometry and functional significance, whereas results of analysis in the left anterior oblique projection did not correlate as well. It was presumed that the problem was due, at least in
part, to foreshortening of the proximal left anterior descending coronary artery on the left anterior oblique angiograms, which at the time of the study were recorded without caudocranial angulation. The data in our current study, in which obviously foreshortened vessels were excluded, strengthen this presumption. Angulation of the vessel relative to the image intensifier, resulting in foreshortening, should produce a rather predictable increase in videodensitometric values. Therefore, the degree of vessel angulation present in selected views of the coronary angiogram and the effect of vessel angulation on the results of videodensitometry need to be further analyzed.

Our current method is also limited by the fact that results are reported in terms of optical density units rather than absolute luminal cross-sectional area. Potential approaches to the derivation of absolute luminal areas by videodensitometry include: (1) the use of a contrast-filled calibration catheter or (2) comparison of the density value of the narrowed coronary segment to that of a normal appearing segment whose luminal size could more easily be determined by quantitative angiographic techniques. However, even if a method is devised that allows the determination of absolute coronary luminal cross-sectional area by videodensitometry, this defined area must then be compared with the normal area for that vessel in that particular patient to determine the true severity of the coronary disease. Defining this normal area may be problematic, because the caliber of the normal coronary tree varies at different portions in its branching structure, and is also related to patient gender.

Thus, the usefulness of knowing absolute coronary luminal area, defined by videodensitometry or any other quantitative technique, depends on knowledge of the normal size of the artery under study in an individual patient. In addition, Kirkeeide et al. have emphasized that minimum luminal area is only one of the geometric characteristics influencing coronary flow reserve and that other lesion characteristics may also need to be considered to accurately predict coronary lesion functional significance.

The particular approach that we have used — the videodensitometric analysis of cineangiograms of coronary stenoses — has limitations in addition to those mentioned above. First, the digitization of angiographic frames increases the time required for videodensitometric analysis. This step would not be required if digitally acquired angiograms were analyzed. In addition, variabilities in film processing could contribute to inaccuracies in the data. Despite these limitations of film-based videodensitometry we used it for two reasons. First, most clinical catheterization laboratories still use angiographic film so the methods we used, if further refined and simplified, could be applied clinically. In addition, at the time this study was done, we did not have the capability of performing digital coronary angiograms in our laboratory.

Limitations of high-frequency echocardiography. We have previously shown (using histology and sonomicrometry) that high-frequency epicardial echocardiography can be used to accurately determine coronary luminal diameters and areas in open-chest animals and postmortem human hearts. The reproducibility of high-frequency echocardiographic determinations of coronary luminal diameters is good, with an intraobserver correlation of \( r = 0.99 \) and an interobserver correlation of \( r = 0.97 \) for 10 human coronary arteries in vitro. In a separate study, the interobserver reproducibility of measurements of luminal area of dog coronary arteries in vivo was also found to be good (\( r = 0.95, y = 0.99x + 0.14, n = 58 \)). However, there are problems inherent in the echocardiographic technique that may have influenced the results of our study. Ultrasound images characteristically have poor lateral resolution. Therefore, only images with clearly visualized lateral walls were analyzed in our study. The ultrasonic probe was hand-held, and although care was taken to rotate the transducer 90 degrees from the long-axis image of the artery to obtain true arterial cross sections, this does not exclude the possibility that some of the images analyzed may have been slightly oblique. It is also possible that despite analysis of the echocardiographic image of the apparently smallest lumen, the actual minimum luminal area may have been missed. Finally, the size of the current probe limits echocardiographic analysis to the left anterior descending and right coronary arteries.

Limitations of the study protocol. First, although we included only angiographically discrete coronary arterial stenoses for analysis of luminal areas to allow close matching of the segments analyzed by videodensitometry and echocardiography, any mismatch of the segments analyzed would be problematic. Second, any differences in medical therapy (i.e., coronary vasodilators such as nitrates or calcium-channel blockers) between the time of catheterization and the time of surgery could have introduced variability into our results. Sixteen of the patients did receive nitroglycerin and/or nifedipine in the cardiac catheterization laboratory, and coronary luminal areas do increase in response to such medications. In addition, although

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medical therapy at the time of cardiac catheterization and surgery was similar, there was a trend toward increased antianginal therapy before coronary bypass surgery. Third, differences in the hemodynamics (i.e., distending pressures) at catheterization vs surgery could have influenced coronary arterial luminal size. However, for the entire patient group, pulse rate and blood pressure did not differ significantly between the time of coronary angiography and the high-frequency echocardiographic studies. Finally, although the time between angiography and surgery was short (less than 1 month in all but three patients), disease progression and/or regression or propagation of thrombus could have resulted in a change in luminal size between the time of catheterization and the echocardiographic studies. Several of these factors, as well as limitations of each technique as delineated above, probably contributed to the variability in our correlation of data derived by videodensitometry with luminal areas defined by high-frequency echocardiography.

Clinical implications. A need exists for a rapid and clinically feasible method of quantitative angiographic analysis to allow the prediction of the geometry and physiologic significance of stenoses seen on human coronary angiograms. Although the angiogram remains the standard by which clinical decisions are made in patients with coronary artery disease, the common clinical method of angiographic analysis, that of estimating percent diameter stenosis, does not represent an optimal method of interpretation.\(^1\)\(^-\)\(^4\),\(^6\),\(^7\) Although rapid, quantitative analysis of all coronary angiograms would be ideal, such analysis may be particularly important for the evaluation of lesions seen on angiograms obtained during interventional cardiologic procedures such as thrombolysis and angioplasty. Harrison et al.\(^37\) have shown that the residual luminal area after thrombolysis could be used to predict the likelihood of reocclusion, and therefore the likelihood of the necessity of proceeding on an emergency basis to angioplasty or bypass surgery to maintain vessel patency. Serruys et al.,\(^38\) as well as our group,\(^9\) have shown the usefulness of videodensitometric analysis during and after percutaneous transluminal coronary angioplasty. Therefore, if the videodensitometric method can be made even more efficient, and particularly if further validation of its accuracy in the analysis of digitally acquired human coronary angiographic images becomes available, videodensitometry could allow critical therapeutic decisions to be made in the cardiac catheterization laboratory rather than hours or days later when angiograms can be analyzed by other sophisticated quantitative analysis procedures.

In summary, this study further validates the ability of videodensitometry to provide an index of coronary luminal area, one of the important determinants of the physiologic significance of a lesion. It also confirms in vivo the assumptions that the results of videodensitometric analysis are independent of angiographic projection and luminal shape. Further studies evaluating this method of angiographic analysis, and particularly evaluating some of the limitations of the method as it is now used, are appropriate and will be necessary before broad clinical application can be encouraged.

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